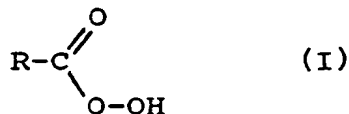




INTERNATIONAL APPLICATION PUBLISHED UNDER THE PATENT COOPERATION TREATY (PCT)

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<p>(21) International Application Number: PCT/DK90/00235</p> <p>(22) International Filing Date: 12 September 1990 (12.09.90)</p> <p>(30) Priority data: 4503/89 12 September 1989 (12.09.89) DK 1737/90 20 July 1990 (20.07.90) DK</p> <p>(71) Applicant (for all designated States except US): NOVO NORDISK A/S [DK/DK]; Novo Alle, DK-2880 Bagsvaerd (DK).</p> <p>(72) Inventors; and</p> <p>(75) Inventors/Applicants (for US only) : KIRK, Ole [DK/DK]; Stefansgade 38, 3.tv., DK-2200 København N (DK). BJÖRKLING, Frederik [SE/SE]; Hövitsmansgatan 2, S-25237 Helsingborg (SE). GODTFREDSSEN, Sven, Erik [DK/DK]; Smedegade 15B, DK-3500 Værløse (DK).</p>		<p>(74) Common Representative: NOVO NORDISK A/S; Patent Department, Novo Alle, DK-2880 Bagsvaerd (DK).</p> <p>(81) Designated States: AT (European patent), AU, BE (European patent), CA, CH (European patent), DE (European patent)*, DK (European patent), ES (European patent), FI, FR (European patent), GB (European patent), IT (European patent), JP, KR, LU (European patent), NL (European patent), SE (European patent), US.</p> <p>Published <i>With international search report.</i></p>

(54) Title: A PROCESS FOR PREPARING PEROXYCARBOXYLIC ACIDS USING AN ENZYME CATALYST



(57) Abstract

A process for the preparation of a peroxycarboxylic acid of general formula (I), wherein R is an organic residue, in particular a linear or branched alkyl group, an aryl group or an alkyl aryl group each of which is optionally substituted with one or more groups, the process comprising treating a carboxylic acid of the general formula R-COOH, wherein R has the meaning indicated above, with hydrogen peroxide or a precursor thereof in the presence of an enzyme catalyst is described. The enzyme catalyst is preferably a hydrolase, such as a protease or a lipase. Also, a process for the oxidation of organic compounds with the peroxycarboxylic acids thus prepared is described.

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A process for preparing peroxycarboxylic acids using an enzyme catalyst.

FIELD OF INVENTION

The present invention relates to a novel process for the preparation of peroxycarboxylic acids. Also, the present invention relates to a process for the oxidation of organic compounds with the peroxycarboxylic acids thus prepared.

BACKGROUND OF THE INVENTION

Peroxycarboxylic acids are commonly employed as oxidizing reagents in the field of organic synthesis for the production of organic chemicals. A wide variety of organic molecules may be oxidized by means of these reagents which, for instance, are useful for the preparation of epoxides from unsaturated hydrocarbons. The various uses of peroxycarboxylic acids are exhaustively described in the art, e.g. in Comprehensive Organic Chemistry edited by Barton and Ollis, Pergamon Press, 1979. Some peroxycarboxylic acids such as meta-chloro-peroxybenzoic acid have become commercially available as a result of their wide applicability.

Even though some peroxycarboxylic acids are useful and commercially available reagents their use is limited because of their relatively high cost and the risks (in particular the explosion hazard) involved in handling the reagents, especially when this is done on a large scale. Accordingly, there is a need for improved methods of preparing peroxycarboxylic acids as well as for methods which make it safer to use them in organic synthesis.

DISCLOSURE OF THE INVENTION

It has surprisingly been found that peroxycarboxylic acids may be generated by treating carboxylic acids with hydrogen peroxide in the presence of an enzyme. This method of preparing peroxycarboxylic acids presents a safe and economically viable approach for the preparation of these highly useful reagents. It has also been found that enzymatic synthesis of peroxycarboxylic acids and oxidation of organic chemicals by means of peroxycarboxylic acids may be carried out simultaneously.

Accordingly, the present invention relates to a process for the preparation of a peroxycarboxylic acid of the general formula (I)

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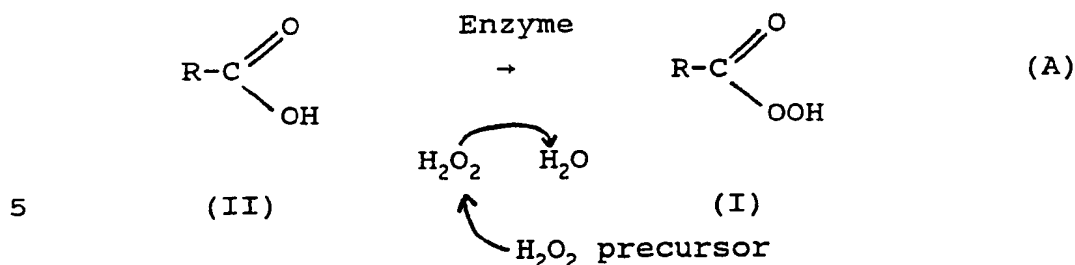


wherein R is an organic residue, in particular a linear or branched, saturated or unsaturated alkyl group, an aryl group or an alkyl aryl group each of which may optionally be substituted with one or more hydroxy, thio, alkyloxy, alcoxy, nitro, oxy, keto, oxo, halo or carboxy groups, the process comprising treating a carboxylic acid of the general formula (II)



wherein R has the meaning indicated above, with hydrogen peroxide or a precursor thereof in the presence of an enzyme catalyst.

The process of the invention may be summarized as indicated in Reaction Scheme (A):



In Reaction Scheme (A), R is as defined above. In particular, R may be alkyl with 1-30 carbon atoms, in particular linear alkyl with 1-8 carbon atoms, or optionally substituted phenyl. If the carboxylic acid substrate (II) is an optically active carboxylic acid, one may employ a racemate or either of the enantiomer forms of the carboxylic acid substrate (II) in the process of the invention.

The enzyme catalyst employed in the process of the invention is preferably a hydrolytic enzyme such as a protease or a lipase. The suitability of a given enzyme for use in the present process may easily be tested by exposing a carboxylic acid substrate to hydrogen peroxide or a hydrogen peroxide precursor in the presence of the enzyme and by monitoring the generation of peroxycarboxylic acid from the reaction. The enzyme may be used as such, but it may also be chemically modified or immobilised in order to enhance its stability and its activity towards the substrate in question.

Lipases which may be employed in the present process may be microbial lipases produced, for instance, by strains of Aspergillus, Enterobacterium, Chromobacterium, Geotrichium or Penicillium. Preferred lipases for use according to the invention are those produced by species of Mucor, Humicola, Pseudomonas or Candida.

Particularly preferred lipases are those produced by the following strains of microorganisms, all of which have been

deposited in the Deutsche Sammlung von Mikroorganismen in accordance with the provisions of the Budapest Treaty on the International Recognition of the Deposit of Microorganisms for the purposes of Patent Procedure:

- 5 Candida antarctica, deposited on 29 September 1986, with the number DSM 3855, and on 8 December 1986, with the numbers DSM 3908 and DSM 3909.
- Pseudomonas cephalica, deposited on 30 January 1987, with the number 3959.
- 10 Humicola lanuginosa, deposited on 13 August 1986 and 4 May, 1987 with the deposit numbers 3819 and 4109, respectively.
- Humicola brevispora, deposited on 4 May 1987, with the deposit number DMS 4110,
- Humicola brevis var. thermoidea, deposited on 4 May 1987,
- 15 with the deposit number DSM 4111, and
- Humicola insolens, deposited on 1 October 1981, with the deposit number DSM 1800.

Currently preferred lipases are those produced by Candida antarctica, DSM 3855, DSM 3908 and DSM 3909. These enzymes

20 may be produced by the process disclosed in WO 88/02775. Briefly, the Candida strains in question may be cultivated under aerobic conditions in a nutrient medium containing assimilable carbon and nitrogen sources as well as essential minerals, trace elements etc., the medium being composed

25 according to established practice. After cultivation, liquid enzyme concentrates may be prepared by removing insoluble materials, e.g. by filtration or centrifugation, after which the culture broth may be concentrated by evaporation or reverse osmosis. Solid enzyme preparations may be prepared

30 from the concentrate by precipitation with salts or water-miscible solvents, e.g. ethanol, or by drying such as spray-drying in accordance with well-known methods.

Additional lipases may be obtained from the following strains which are publicly available without restriction from the

35 Centraalbureau voor Schimmelculturen (CBS), American Type

Culture Collection (ATCC), Agricultural Research Culture Collection (NRRL) and Institute of Fermentation, Osaka (IFO) with the following deposit numbers: Candida antarctica, CBS 5955, ATCC 34888, NRRL Y-8295, CBS 6678, ATCC 28323, CBS 6821
5 and NRRL Y-7954; Candida tsukubaensis, CBS 6389, ATCC 24555 and NRRL Y-7795; Candida auriculariae, CBS 6379, ATCC 24121 and IFO 1580; Candida humicola, CBS 571, ATCC 14438, IFO 0760, CBS 2041, ATCC 9949, NRRL Y-1266, IFO 0753 and IFO 1527; and Candida foliorum, CBS 5234 and ATCC 18820.

- 10 It is known to produce lipase by recombinant DNA techniques, cf. for instance EP 238 023. Recombinant lipases may also be employed for the present purpose.

When employed in the process of the invention, the enzyme may be in a soluble state. It is, however, preferred to immobi-
15 lize the enzyme in order to facilitate the recovery of the peroxycarboxylic acids produced by the present process. Immobilization procedures are well known (cf. for instance K. Mosbach, ed., "Immobilized Enzymes", Methods in Enzymology 44, Academic Press, New York, 1976) and include cross-linking
20 of cell homogenates, covalent coupling to insoluble organic or inorganic supports, entrapment in gels and adsorption to ion exchange resins or other adsorbent materials. Coating on a particulate support may also be employed (cf. for instance A.R. Macrae and R.C. Hammond, Biotechnology and Genetic
25 Engineering Reviews 3, 1985, p. 193. Suitable support materials for the immobilized enzyme are, for instance, plastics (e.g. polypropylene, polystyrene, polyvinylchloride, polyurethane, latex, nylon, teflon, dacron, polyvinylacetate, polyvinylalcohol or any suitable copolymer thereof), polysac-
30 charides (e.g. agarose or dextran), ion exchange resins (both cation and anion exchange resins), silicon polymers (e.g. siloxane) or silicates (e.g. glass).

It is preferred to immobilize the enzyme on an ion exchange resin by adsorbing the enzyme to the resin or by cross-

linking it to the resin by means of glutaraldehyde or another cross-linking agent in a manner known per se. A particularly preferred resin is a weakly basic anion exchange resin which may be a polystyrene-, acrylic- or phenol-formaldehyde-type resin. Examples of commercially available polyacrylic-type resins are Lewatit E 1999/85 (registered trademark of Bayer, Federal Republic of Germany) and Duolite ES-568 (registered trademark of Rohm & Haas, FRG). Immobilization of enzymes to this type of resin may be carried out according to EP 140 542. Immobilization to phenyl-formaldehyde-type resins may be done according to DK 85/878. An example of a commercially available acrylic-type resin is Lewatit E2001/85 (registered trademark of Bayer, FRG).

Another convenient material for immobilizing enzymes is an inorganic support, such as a silicate. The enzyme may be attached to the support by adsorption or by covalent coupling, eg. as described in K. Mosbach, ed., op.cit.

The process according to the method of the invention may be carried out in the carboxylic acid substrate itself (which in this case also acts as a solvent) or in solvents such as water, aqueous buffer solutions or organic solvents. Some preferred organic solvents are hydrocarbons such as hexane, cyclohexane, heptane, benzene and toluene, methylene chloride and hexachloroethene, or acetonitrile, dimethylformamide, dioxane and tetrahydrofuran. It is preferred to employ solvents in which the substrate and products of the reaction are highly soluble and in which the enzyme maintains a good stability and activity.

If an organic substance e.g. an alkene is to be oxidized in situ by the Peroxycarboxylic acid being formed, this substance may advantageously be used as the solvent.

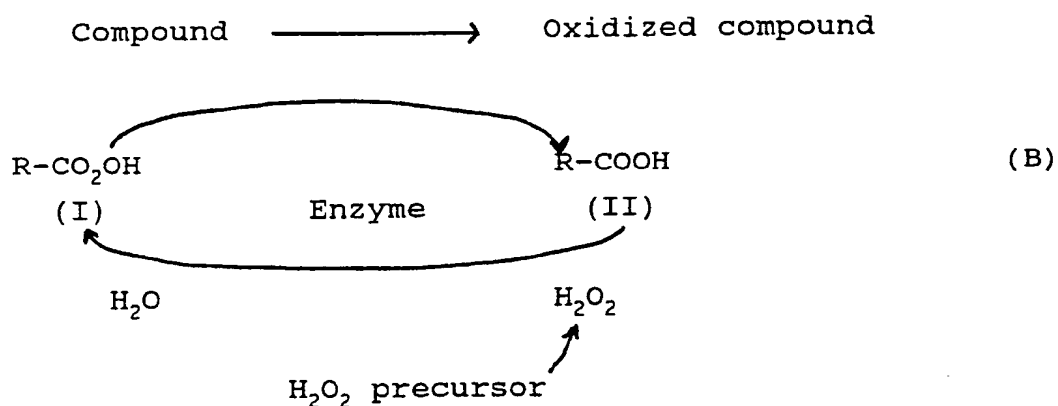
The temperature at which the reaction of the carboxylic acid (II) takes place is not critical, but is conveniently in the range of about 20-100 °C, such as about 30-80 °C.

The hydrogen peroxide employed according to the process of the invention may be added as such to the reaction mixture either at the beginning of the reaction or at a desired rate in the course of the reaction. Alternatively, it is possible to employ a precursor of hydrogen peroxide such precursors being compounds which give rise to the formation of hydrogen peroxide in situ, such as percarbonates or perborates.

The water generated in the course of the process according to the invention may, if desired, be removed by methods known in the art such as by distillation, exposure to dessicants etc.

As indicated above, it has surprisingly been found that the process of the present invention may be carried out concomitantly with oxidation of an organic compound susceptible to oxidation with peroxycarboxylic acids as indicated in Reaction Scheme (B) below:

20



In Reaction Scheme (B) the "compound" may be any compound susceptible to peroxycarboxylic acid oxidation, e.g. an unsaturated hydrocarbon or a sulphur-containing organic

molecule, while "R", "Enzyme" and "H₂O₂-precursor" have the meanings indicated above.

The process of the invention shown in Reaction Scheme (B) above may be carried out using substantially equimolar
5 amounts of the "compound" and the carboxylic acid substrate (II). If desired, however, the process may be carried out using less than equimolar amounts of the carboxylic acid (II) since this compound will be regenerated in the course of the reaction as indicated in Reaction Scheme (B).

10 The process shown in Reaction Scheme (B) makes it unnecessary to transport and handle large quantities of peroxy-carboxylic acids so that the hazards involved in using these oxidants are greatly reduced.

Furthermore, as indicated above, the carboxylic acid (II) may
15 be prochiral or chiral and, in such instances, employed as a racemate or as either of its optically active stereoisomers. In cases, where the "compound" is prochiral or chiral, the carboxylic acid substrate (II) and the enzyme may be so selected that the "oxidized compound" is generated in a
20 desired optically active form or as a racemate. The process of the invention may thus be employed for the synthesis of optically active compounds.

The process shown in Reaction Scheme (B) has for instance been found to be advantageous in the preparation of epoxides
25 from alkenes.

The process of the invention is further illustrated in the following non-limiting examples.

General procedures :

Peroxy-carboxylic acid references were prepared according to
30 W. E. Parker, C. Ricciuti, C. L. Ogg and D. Swern, J. Am.

Chem. Soc. 77, 4037 (1955). Peroxycarboxylic acid production was monitored by means of HPLC (Merck LiChrosorb RP-18 column, MeOH/H₂O/HCOOH ; 70/30/0.1, and UV-detector). Reactions were monitored by means of capillary gas chromatography.

5 Example 1.

To a stirred solution of octanoic acid (720 mg, 5 mmol) in hexane (50 ml) was added immobilized lipase derived from Candida antarctica (1 g, prepared according to examples 1 and 19 of WO 88/02775) and hydrogen peroxide (170 mg, 5 mmol, 10 added as 510 μ l 30 % solution). After the reaction mixture had been refluxed for 30 min, HPLC analysis showed a peroxy-octanoic acid concentration of 43 mM (43 % conversion).

Example 2.

Octanoic acid was oxidized as described in example 1 with the 15 exception that acetonitrile was used as the solvent. After 30 min, 15 mM peroxyoctanoic acid was detected.

Example 3.

Example 1 was repeated in the presence of either 10 mM styrene or 10 mM 1,2-epoxyethylbenzene. In both cases, a peroxy- 20 carboxylic acid production which was comparable to that of example 1 was observed. Thus the enzyme did not appear to be inhibited by either of these compounds.

Example 4:

Preparation of styrene oxide:

25 To a stirred suspension (at room temperature) of immobilized C. antartica lipase (370 mg, according to example 1) in styrene (4.15 ml, 36.1 mmol) containing myristic acid (823 mg, 3.6 mmol) hydrogen peroxide (3 ml, 52.5 mmol) was added in six equal portions after 0, 0.5, 1.0, 1.5, 2.0 and 3.0

hours. After 1.5 hours 16.5% styrene oxide was formed as determined by gas chromatography.

Example 5.

Peroxycarboxylic acids were prepared from various carboxylic acids (see Table 1) as follows:

To a solution of carboxylic acid (630mM, 3.15 mmol) in toluene (5 ml) was added immobilized *C. antarctica* lipase (100 mg, as described in example 1) and hydrogen peroxide (255 μ l, 60% (w/v), 4.45 mmol), with stirring. The reaction was allowed to proceed at room temperature for 120 minutes after which the yield of peroxycarboxylic acid was determined by RP-18 HPLC. The results are shown in Table 1 below.

Table 1

<u>Carboxylic acid</u>	<u>mM peroxycarboxylic acid</u>
15 Hexanoic acid	228
Octanoic acid	236*
Decanoic acid	249
Dodecanoic acid	270
Tetradecanoic acid	277
20 Hexadecanoic acid	271
Octadecanoic acid	170

* In this case, xylene was used as the solvent due to interference by toluene in the assay.

Example 6

25 Epoxides were prepared from various alkenes (cf. Table 2) as follows:

To a stirred suspension of immobilized *C. antarctica* lipase (100 mg, as described in example 1) in a solution of hexane (10 ml), alkene (10mM) and octanoic acid (10mM) was added hydrogen peroxide (25 μ l, 0.05 mmol, 60%) at room temperature. The reaction was allowed to proceed for 4 hours after which the yield of epoxide was determined by capillary gas chromatography.

To compare, 10mM preformed peroxyoctanoic acid (prepared as described in D. Sweern, Organic Peroxides 2, Ch. 5, Wiley Interscience, New York, 1971; GB 1 452 730; W.E. Parker et al., J. Amer. Chem. Soc. 79, 1957 p. 1929) was added to 10 ml of a 10 mM solution of alkene in hexane. The reaction time in this experiment was also 4 hours. The yield of epoxide was determined as indicated above.

15 The results are shown in Table 2 below.

Table 2

<u>Alkene</u>	<u>% Yield</u>	
	<u>Catalytic oxidation</u>	<u>Chemical oxidation</u>
Cyclohexene	2	10
20 3-Ethyl-2-pentene	48	50
Tetramethylethylene	99	74

Example 7

Epoxides were prepared from various alkenes (cf. Fig. 1) in a solvent-free medium as follows:

25 To a stirred suspension of immobilized *C. antarctica* lipase (175 mg, as described in example 1) in alkene (1.75 ml, about 15 mmol) containing octanoic acid (270 μ l, 1.7 μ mol) was added hydrogen peroxide (235 μ l, 60% w/v) at the beginning of the reaction and after 1, 1.5, 2.5 and 4 hours (20 mmol in 30 all). Yields were determined by capillary gas chromatography.

The results are shown in Fig. 1, in which \diamond is cyclohexene, x is 3-ethyl-2-pentene, ∇ is tetramethylethylene, and \square is 1-octene.

Example 8:

5 Preparation of hexadecene oxide, method A :

A mechanically stirred suspension of immobilized C. antartica lipase (1 g, according to example 1) in 1-hexadecene (15 ml, ca. 52.4 mmol) containing myristic acid (1.2 g, 5.25 mmol) was heated to 50°C. To this mixture hydrogen peroxide (4.6 ml
10 60% (w/v)) was added in four equal portions after 0, 1.5, 3 and 4.5 hours (80.5 mmol in all). After 20 hours reaction time 51% hexadecene oxide was formed as determined by gas chromatography.

^1H NMR: δ = 2.88-2.93 (m, 1H), 2.72-2.76 (dd, 1H), 2.45-2.49
15 (dd, 1H), 1.5-1.55 (m, 2H), 1.42-1.48 (m, 2H), 1.25-1.32 (m, 22H), 0.89 (t, 3H)

Example 9:

Preparation of hexadecene oxide, method B:

A mechanically stirred suspension of immobilized C. antartica
20 lipase (1 g, according to example 1) in 1-hexadecene (15 ml, ca. 52.4 mmol) containing myristic acid (3.0 g, 13.1 mmol) was heated to 50°C. To this mixture hydrogen peroxide (4.6 ml 60% (w/v)) was added in four equal portions after 0, 1.5, 3 and 4.5 hours (80.5 mmol in all). After 24 hours reaction
25 time 79.4 % hexadecene oxide was formed as determined by gas chromatography.

^1H NMR: δ = 2.88-2.93 (m, 1H), 2.72-2.76 (dd, 1H), 2.45-2.49 (dd, 1H), 1.5-1.55 (m, 2H), 1.42-1.48 (m, 2H), 1.25-1.32 (m, 22H), 0.89 (t, 3H)

30 Example 10:

Preparation of octene oxide, method A:

A mechanically stirred suspension of immobilized C. antartica lipase (100 mg, according to example 1) in toluene (13.5 ml), 1-octene (1.5 ml, 9.54 mmol) and myristic acid (0.22 g, 0.95 mmol) was heated to 50°C. To this mixture hydrogen peroxide (0.8 ml, 60% (w/v)) was added in four equal portions after 0, 1.5, 3 and 4.5 hours (14 mmol in all). After 24 hours 35% octene oxide was formed as determined by gas chromatography.
¹H NMR: δ= 2.87-2.96 (m, 1H), 2.73-2.78 (dd, 1H), 2.45-2.49 (dd, 1H), 1.5-1.57 (m, 2H), 1.43-1.49 (m, 2H), 1.27-1.39 (m, 6H), 0.9 (t, 3H)

Example 11:

Preparation of octene oxide, method B:

To a mechanically stirred suspension (50°C) of immobilized C. antartica lipase (1 g, according to example 1) in 1-octene (15 ml, ca.95.4 mmol) containing myristic acid (4.356 g, 19.1 mmol) was hydrogen peroxide (8 ml 60% (w/v)) added in four equal portions after 0, 1.5, 3 and 4.5 hours (140 mmol in all). After 6 hours 51% octene oxide was formed as determined by gas chromatography.
¹H NMR: δ= 2.87-2.96 (m, 1H), 2.73-2.78 (dd, 1H), 2.45-2.49 (dd, 1H), 1.5-1.57 (m, 2H), 1.43-1.49 (m, 2H), 1.27-1.39 (m, 6H), 0.9 (t, 3H)

Example 12:

Preparation of methylene cyclohexane oxide :

To a stirred suspension (at room temperature) of immobilized C. antartica lipase (24 mg, according to example 1) in toluene (3 ml), methylene cyclohexane (0.24 ml, 2 mmol) and myristic acid (46mg), was hydrogen peroxide (0.175 ml 60% (w/v)) added in five equal portions after 0, 1, 2, 3 and 4 hours. After 24 hours 97% methylene cyclohexane oxide was formed as determined by gas chromatography.

Example 13:

Preparation of penicillin V sulfoxide :

To a mechanically stirred suspension of immobilized C. antarctica lipase (150 mg, according to example 1) in toluene (15 ml) and myristic acid (1 g, 4.6 mmol), was hydrogen peroxide (1.2 ml 60% (w/v), 21 mmol in all) added in four equal portions after 0, 2, 3 and 4 hours. Penicillin V-potassium salt (2.4 g, 6.2 mmol in all) was added in three equal portions after 2, 3 and 4 hours. The yields were determined by HPLC (Column: Supelco RP-18 ,5 micro; Mobile phase: Acetonitrile 20% and pH 6.5 Phosphate buffer 80%; Flow: 1ml/min. UV-detector). Full turnover was reached after 5 hours total reaction time.

Example 14:

15 Preparation of didodecane disulfide:

To a suspension of immobilized C. antarctica lipase (100 mg, according to example 1) in toluene (5 ml), dodecanthiol (1.18 ml, 4.9 mmol) and myristic acid (1.12 g) was added hydrogen peroxide (0.28 ml 60% (w/v)). Product formed (Tlc, ethylacetate).

Example 15:

Preparation of δ -valerolactone:

To a stirred suspension (at room temperature) of immobilized C. antarctica lipase (100 mg, according to example 1) in toluene (3 ml), cyclopentanone (0.265 ml, 3 mmol) and myristic acid (228 mg), was hydrogen peroxide (0.5 ml 60% w/v, 8.75 mmol) added. After 20 hours 16% δ -valerolactone was formed as determined by gas chromatography.

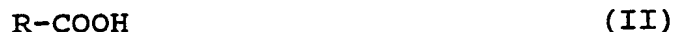
CLAIMS

1. A process for the preparation of a peroxycarboxylic acid of the general formula (I)

5



wherein R is an organic residue, in particular a linear or branched alkyl group, an aryl group or an alkyl aryl group each of which is optionally substituted with one or more
10 hydroxy, thio, alkyloxy, alkoxy, nitro, oxy, keto, oxo, halo or carboxy groups, the process comprising treating a carboxylic acid of the general formula (II)



wherein R has the meaning indicated above, with hydrogen,
15 peroxide or a precursor thereof in the presence of an enzyme catalyst.

2. A process according to claim 1, wherein the enzyme catalyst is a hydrolase.

20 3. A process according to claim 2, wherein the hydrolase is a protease or a lipase.
4. A process according to claim 3, wherein the enzyme is a microbial enzyme.

5. A process according to claim 4, wherein the enzyme is a bacterial enzyme.

25 6. A process according to claim 5, wherein the lipase is one obtainable from a species of Pseudomonas.

7. A process according to claim 6, wherein the lipase is one obtainable from Pseudomonas cephalica, DSM 3959.
8. A process according to claim 4, wherein the enzyme is a fungal enzyme.
- 5 9. A process according to claim 8, wherein the lipase is one obtainable from a species of Mucor, Aspergillus, Humicola, or Candida.
10. A process according to claim 9, wherein the lipase is one obtainable from Candida antarctica, DSM 3855, DSM 3908 or DSM
10 3909, Humicola lanuginosa, DSM 3819 or DSM 4109, Humicola brevispora, DSM 4110, Humicola brevis var. thermoidea, DSM 4111, or Humicola insolens, DSM 1800.
11. A process according to any of the preceding claims, wherein the enzyme is an immobilized enzyme.
- 15 12. A process according to any of the preceding claims, wherein the reaction is carried out in an organic solvent.
13. A process according to any of the preceding claims, wherein R is alkyl with 1-30 carbon atoms, in particular linear alkyl with 1-8 carbon atoms, or optionally substituted
20 phenyl.
14. A process according to any of the preceding claims, wherein R is chiral or prochiral.
15. A process for the oxidation of organic compounds by means of a peroxycarboxylic acid, wherein the peroxycarboxylic acid
25 is generated by the process according to any of claims 1-14.
16. A process according to claim 15, wherein the peroxycarboxylic acid is generated in situ.

17. A process according to claim 15 or 16, wherein the organic compound is an alkene.

18. A process according to any of the claims 15 to 17, wherein the process is carried out using one or more of the 5 reactants as solvent.

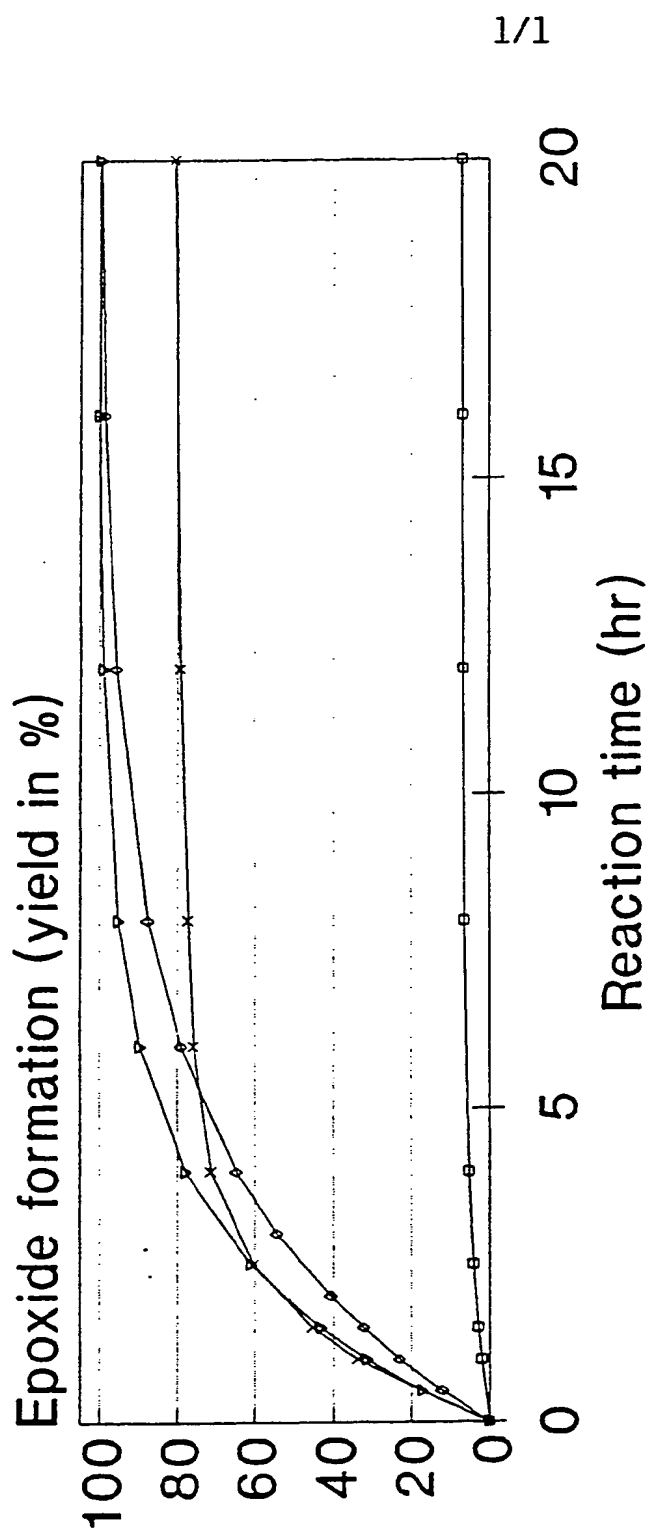


Figure 1

INTERNATIONAL SEARCH REPORT

International Application No. **PCT/DK 90/00235**

I. CLASSIFICATION OF SUBJECT MATTER (if several classification symbols apply, indicate all) ⁶ According to International Patent Classification (IPC) or to both National Classification and IPC IPC5: C 12 P 7/40, 7/00 // C 07 D 301/16											
II. FIELDS SEARCHED <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black;">Minimum Documentation Searched⁷</div> <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 20%; border-bottom: 1px solid black;">Classification System</th> <th style="border-bottom: 1px solid black;">Classification Symbols</th> </tr> <tr> <td style="height: 40px; vertical-align: bottom; border-right: 1px solid black;">IPC5</td> <td>C 12 P</td> </tr> </table> <div style="text-align: center; border-top: 1px solid black; border-bottom: 1px solid black;">Documentation Searched other than Minimum Documentation to the Extent that such Documents are Included in Fields Searched⁸</div> <p>SE,DK,FI,NO classes as above</p>			Classification System	Classification Symbols	IPC5	C 12 P					
Classification System	Classification Symbols										
IPC5	C 12 P										
III. DOCUMENTS CONSIDERED TO BE RELEVANT⁹ <table style="width: 100%; border-collapse: collapse;"> <tr> <th style="width: 10%; border-bottom: 1px solid black;">Category *</th> <th style="border-bottom: 1px solid black;">Citation of Document,¹¹ with indication, where appropriate, of the relevant passages¹²</th> <th style="width: 15%; border-bottom: 1px solid black;">Relevant to Claim No.¹³</th> </tr> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td>EP, A2, 0310952 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN) 12 April 1989, see esp. page 2, lines 6-43 ---</td> <td style="text-align: center; vertical-align: top;">1-18</td> </tr> <tr> <td style="text-align: center; vertical-align: top;">X</td> <td>DE, A, 2240605 (COLGATE-PALMOLIVE CO.) 8 March 1973, see esp. page 3, line 15 - page 4 line 4 -----</td> <td style="text-align: center; vertical-align: top;">1-18</td> </tr> </table>			Category *	Citation of Document, ¹¹ with indication, where appropriate, of the relevant passages ¹²	Relevant to Claim No. ¹³	X	EP, A2, 0310952 (HENKEL KOMMANDITGESELLSCHAFT AUF AKTIEN) 12 April 1989, see esp. page 2, lines 6-43 ---	1-18	X	DE, A, 2240605 (COLGATE-PALMOLIVE CO.) 8 March 1973, see esp. page 3, line 15 - page 4 line 4 -----	1-18
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<div style="display: flex; justify-content: space-between;"> <div style="width: 45%;"> <p>* Special categories of cited documents:¹⁰</p> <p>"A" document defining the general state of the art which is not considered to be of particular relevance</p> <p>"E" earlier document but published on or after the international filing date</p> <p>"L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified)</p> <p>"O" document referring to an oral disclosure, use, exhibition or other means</p> <p>"P" document published prior to the international filing date but later than the priority date claimed</p> </div> <div style="width: 45%;"> <p>"T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention</p> <p>"X" document of particular relevance, the claimed invention cannot be considered novel or cannot be considered to involve an inventive step</p> <p>"Y" document of particular relevance, the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art.</p> <p>"&" document member of the same patent family</p> </div> </div>											
IV. CERTIFICATION <table style="width: 100%; border-collapse: collapse;"> <tr> <td style="width: 50%; border-bottom: 1px solid black;">Date of the Actual Completion of the International Search</td> <td style="width: 50%; border-bottom: 1px solid black;">Date of Mailing of this International Search Report</td> </tr> <tr> <td style="height: 40px; vertical-align: bottom;">10th December 1990</td> <td style="text-align: center; vertical-align: bottom;">1990 -12- 12</td> </tr> <tr> <td style="border-bottom: 1px solid black;">International Searching Authority</td> <td style="border-bottom: 1px solid black;">Signature of Authorized Officer</td> </tr> <tr> <td style="text-align: center; vertical-align: bottom;">SWEDISH PATENT OFFICE</td> <td style="text-align: center; vertical-align: bottom;">Anna Sjölund </td> </tr> </table>			Date of the Actual Completion of the International Search	Date of Mailing of this International Search Report	10th December 1990	1990 -12- 12	International Searching Authority	Signature of Authorized Officer	SWEDISH PATENT OFFICE	Anna Sjölund	
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SWEDISH PATENT OFFICE	Anna Sjölund										

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**ANNEX TO THE INTERNATIONAL SEARCH REPORT
ON INTERNATIONAL PATENT APPLICATION NO. PCT/DK 90/00235**

This annex lists the patent family members relating to the patent documents cited in the above-mentioned international search report. The members are as contained in the Swedish Patent Office EDP file on **90-11-01**.
The Swedish Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent document cited in search report	Publication date	Patent family member(s)	Publication date
EP-A2- 0310952	89-04-12	DE-A- 3734047	89-04-20
		DE-A- 3806403	89-09-07
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DE-A- 2240605	73-03-08	AU-D- 4586172	74-02-28
		BE-A- 787883	72-12-18
		CA-A- 990230	76-06-01
		CH-A- 576516	76-06-15
		FR-A-B- 2150242	73-04-06
		GB-A- 1401312	75-07-16
		NL-A- 7211523	73-02-27